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## Accounting for comorbidity in assessing the burden of epilepsy among US adults: Results from the National Comorbidity Survey Replication (NCS-R)

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### Abstract

Although epilepsy is associated with substantial role impairment, it is also highly comorbid with other physical and mental disorders, making unclear the extent to which impairments associated with epilepsy are actually due to comorbidities. This issue was explored in the National Comorbidity Survey Replication (NCS-R), a nationally representative household survey of 5,692 US adults. Medically-recognized epilepsy was ascertained with self-report, comorbid physical disorders with a chronic conditions checklist, and comorbid DSM-IV mental disorders with the Composite International Diagnostic Interview (CIDI). Lifetime epilepsy prevalence was estimated at 1.8%. Epilepsy was comorbid with numerous neurological and general medical conditions and with a sporadic cluster of mental comorbidities (panic, PTSD, conduct disorder, and substance use disorders). Although comorbid disorders explain part of the significant gross associations of epilepsy with impairment, epilepsy remains significantly associated with work disability, cognitive impairment, and days of role impairment after controlling comorbidities. The net association of epilepsy with days of role impairment after controlling for comorbidities is equivalent to an annualized 89.4 million excess role impairment days among US adults with epilepsy, arguing that role impairment is a major component of the societal costs of epilepsy per se rather than merely due to disorders comorbid with epilepsy. This estimated burden is likely conservative as some parts of the effects of epilepsy are presumably mediated by secondary comorbid disorders.

### Keywords

epilepsy; seizure; epidemiology; comorbidity; role impairment; nosology

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### DISCLOSURE OF CONFLICTS OF INTEREST

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## INTRODUCTION

Epilepsy is among the most prevalent of the serious neurological disorders, affecting roughly 50 million people worldwide<sup>1, 2</sup> and 2.1–2.7 million Americans.<sup>3</sup> Its burden cascades beyond the immediate central nervous system dysfunction of the disorder per se to a number of neurobehavioral impairments, role disabilities, and psychosocial disadvantages.<sup>4</sup> These are associated with substantial economic burdens documented in studies showing that people with epilepsy have significantly lower family incomes than other people; a pattern largely due to the un/underemployment of people with epilepsy.<sup>5</sup>

While estimates of the burden of epilepsy consistently increase in studies that include more textured burden measures,<sup>6</sup> these studies are limited in usually not adjusting for the wide range of general medical and mental disorders known to be comorbid with epilepsy.<sup>7–10</sup> An evaluation of the extent to which estimates of the burden of epilepsy decrease when comorbidities are controlled would be of considerable value given that targeted interventions to reduce the adverse life course consequences of epilepsy should be guided by information about important pathways that lead to these consequences. The current report addresses this issue with data from the National Comorbidity Survey Replication (NCS-R),<sup>11</sup> a national epidemiological survey. We examine whether self-reported epilepsy is associated with chronic physical and mental disorders and the extent to which the associations of epilepsy with diverse measures of role impairment are explained by comorbid disorders.

## MATERIALS AND METHODS

### Sample

The NCS-R was a face-to-face household survey of English-speaking adults (ages 18+) carried out between February 2001 and April 2003 in a multi-stage clustered area probability sample of the US population. A detailed description of the NCS-R sample design is presented elsewhere.<sup>12</sup> The primary sampling areas (PSAs) [Census Metropolitan Statistical Areas (MSAs) and non-MSA counties] were selected with stratification to guarantee representativeness of the US population on a wide range of geographic and socio-demographic characteristics. Recruitment of respondents within clustered probability samples of households inside PSAs began with an advance letter and study fact brochure followed by in-person interviewer visits to explain study aims and procedures, randomly select a respondent, and obtain informed consent before administering the interview. Respondents were paid \$50 for participation. The response rate was 70.9%. A probability sub-sample of non-respondents was then selected and paid \$100 to complete a short non-respondent survey. Recruitment and consent procedures were approved by the human subjects committees of Harvard Medical School and the University of Michigan.

The survey was administered in two parts. Part I included a core diagnostic assessment administered to all respondents (n = 9,282). Part II included questions about correlates and additional disorders administered to all respondents who met lifetime criteria for any Part I disorder plus a probability sub-sample of other Part I respondents (n = 5,692). The Part I sample was weighted to adjust for differential probabilities of selection and minor non-response bias detected in the non-respondent survey. The Part II sample, the focus of the current report due to epilepsy being assessed in Part II, was then additionally weighted for differential probabilities of selection into Part I depending on Part I disorders. A final weight adjusted the Part II sample to match the 2000 census population on the cross-classification of numerous geographic and socio-demographic variables to correct for minor residual discrepancies between sample and population distributions on these variables. All analyses employed these weights. More detailed information about NCS-R sampling, weighting, and socio-demographic distributions is reported elsewhere.<sup>12</sup>

## Measures

**Mental disorders**—The majority of lifetime mental disorders were assessed in Part I. As noted above, these assessments were used to differentially select respondents into Part II, where assessments were made of additional mental disorders as well as of physical disorders. All mental disorders were assessed with the fully-structured lay-administered Composite International Diagnostic Interview (CIDI) Version 3.0.<sup>13</sup> DSM-IV criteria were used with diagnostic hierarchy and organic exclusion rules to make diagnoses of anxiety (panic disorder, generalized anxiety disorder, phobias, PTSD, separation anxiety disorder), mood (major depression, dysthymic disorder, bipolar disorder), disruptive behavior (ADHD, oppositional-defiant disorder, conduct disorder, intermittent explosive disorder), and substance (alcohol and drug abuse and dependence) disorders. Generally good concordance was found between these DSM-IV/CIDI diagnoses and clinical diagnoses in blinded clinical reappraisal interviews.<sup>14</sup>

**Self-reported epilepsy**—All Part II NCS-R respondents were asked: “Did a doctor or other health professional ever tell you that you had epilepsy or seizures?” Virtually identically worded questions have been used to ascertain cases in most other large-scale epidemiological surveys of epilepsy.<sup>8, 15–18</sup> Validation of responses to comparable questions in other community surveys found that 76–89.5% of cases defined by a consensus diagnosis of epilepsy were detected by self-report (sensitivity) and that 66–81.5% of self-reported positives were confirmed by the consensus diagnosis (positive predictive value).<sup>19, 20</sup>

**Comorbid physical disorders**—Lifetime prevalence of common chronic physical disorders was assessed with a Part II chronic conditions checklist<sup>21</sup> based on the checklist in the US National Health Interview Survey.<sup>22</sup> Included were: cardiovascular (heart disease, hypertension, history of heart attack, history of stroke), digestive (irritable bowel disorder, ulcer), musculoskeletal (arthritis, chronic back/neck pain), pain (migraine, other chronic headaches, other chronic pain conditions), respiratory (asthma, seasonal allergies, and other lung conditions like COPD and TB), sensory (blindness, deafness, and serious hearing or vision impairments), and other (cancer, diabetes) disorders. Such checklists, which are widely used in community epidemiologic surveys, have been shown to yield more complete and accurate information than open-ended health questions and to have moderate-high agreement with independent medical records.<sup>23</sup>

**Role Functioning**—All Part II respondents were administered the World Health Organization Disability Assessment Scale (WHO-DAS),<sup>24, 25</sup> a multidimensional self-report inventory of health-related limitations in role functioning during the past 30 days. The 8 WHO-DAS scales include three domains of basic activities of daily living (cognition, mobility, self-care), two of instrumental activities of daily living (productive role functioning, social role functioning), and three of societal response (stigma, discrimination, and family burden). Scores on each WHO-DAS scale were normed to a theoretical 0–100 range. WHO-DAS scales have good internal consistency reliability and predictive validity.<sup>26</sup>

The WHO-DAS scale of productive role functioning included, among other items, three questions of interest in themselves: number of days in the past 30 respondents were totally unable to work or conduct their other daily activities because of health problems; and number of days in the past 30 respondents were able to work but had to cut back either on the quality or quantity of their work because of health problems. Responses to these questions have shown good concordance with independent records of workplace sickness absence in samples of workers.<sup>27</sup> An overall measure of number of impaired performance days was created by summing each day of total role loss (counting as a full day) and each day of reduced work quantity or quality (each counting as half a day).

## Analysis methods

Cross-tabulations and bivariate logistic regression analyses were used to examine socio-demographic correlates of epilepsy and comorbidities, including age, sex, race-ethnicity, education, marital status, and employment status. Multivariate regression analysis was used to examine associations of epilepsy with a dichotomous measure of work disability (logistic regression) and with WHO-DAS scores (linear regression). All regression equations controlled sequentially for socio-demographics, physical comorbidities, mental comorbidities, and all comorbidities. Interaction tests were used to investigate whether associations of epilepsy with the outcomes varied depending on the presence of comorbid conditions. The Taylor series method<sup>28</sup> implemented in SUDAAN Version 8.0.1<sup>29</sup> adjusted results for the clustering and weighting of the NCS-R sample design. Logistic regression coefficients and their standard errors were exponentiated for ease of interpretation and are reported as odds-ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was consistently evaluated using design-based two-sided .05 level tests.

## RESULTS

### Prevalence and socio-demographic correlates

Epilepsy was estimated to have a lifetime prevalence of 1.8% (95% confidence interval: 1.4–2.2) and to be unrelated to age, sex, race-ethnicity, and education. (Results are not reported, but are available on request.) Epilepsy was also estimated to be significantly more common among the never married than the married and among those in the “other” employed category (consisting of the unemployed, disabled, and those neither in the labor force nor homemakers, retired, or students) compared to the employed.

### Comorbidity with physical and mental disorders

Respondents with epilepsy were significantly more likely than others to report at least one of the comorbid physical disorders assessed in the NCS-R (93.6% vs. 77.8%,  $p < .001$ ), with an OR of 4.2 ( $p < .001$ ) after controlling for socio-demographic factors that could not be consequences of epilepsy (age, sex, race-ethnicity). Epilepsy is positively related to all these physical disorders, nearly half with statistically significant ORs (1.6–3.0  $p = .032 - < .001$ ), including with stroke, hearing impairment, vision impairment, asthma, digestive disorders, chronic non-migraine headaches, and arthritis. Interestingly, epilepsy is most strongly related to *high* comorbidity, defined as having 4 or more comorbid physical disorders. Specifically, 41.2% of respondents with epilepsy have high comorbidity compared to 20.2% of other respondents ( $p < .001$ ), while differences in the proportions of people with vs. without epilepsy who have 1–3 comorbid physical disorders are much smaller and inconsistent in sign.

As with physical comorbidities, respondents with epilepsy were significantly more likely than other respondents to report at least one of the DSM-IV/CIDI mental disorders assessed in the survey (67.9% vs. 47.0%,  $p = .011$ ), with an OR of 2.1 ( $p = .011$ ) after controlling for age, sex, and race-ethnicity. (Table 2) Unlike physical disorders, though, the proportional elevation in prevalence of mental disorders among people with vs. without epilepsy does not vary systematically by number of comorbid disorders. Although epilepsy is positively related to the vast majority of these mental disorders, only four associations are statistically significant: with post-traumatic stress disorder, panic disorder, conduct disorder, and drug abuse (OR = 1.8–3.3,  $p = .002-.043$ ).

### Labor force participation

The proportion of respondents in the labor force (i.e., either employed, self-employed, looking for work, or disabled) who reported their employment status as “disabled” is nearly

five times as high among those with than without epilepsy (33.1% vs. 7.0%,  $p < .001$ ). The OR between epilepsy and disability remains significant ( $p < .001$ ) but decreases from 6.6 to 5.7 after controlling for age, sex, race-ethnicity, and education, to 4.1–5.0 after also controlling for physical or mental disorders, and to 3.8 after controlling for both physical and mental disorders. (Table 3) Given the earlier finding of high comorbidity between epilepsy and other disorders, we also evaluated the significance of interactions between epilepsy and number of comorbid physical and mental disorders in predicting disability, but these interactions were not statistically significant ( $p = .19-.58$ ).

### WHO-DAS scores

Respondents with epilepsy reported elevated impairment in all 8 WHO-DAS domains. (Table 4) Seven of the 8 unstandardized linear regression coefficients are significant (the exception being self care), and in the range 1.4–15.8 ( $p = .001-.045$ ) on the 0–100 response scale. All these coefficients become smaller when controls are introduced for socio-demographics and smaller yet when additional controls are included for comorbid physical and mental disorders, with only the impaired cognition coefficient remaining significant when all controls are added (2.4,  $p = .021$ ). Interactions of epilepsy with number of comorbid physical and mental disorders in predicting the 8 WHO-DAS scores are insignificant in 15 of 16 cases ( $p = .15-.93$ ). The exception is a negative interaction ( $p = .018$ ) between epilepsy and number of mental disorders predicting impairment in self-care.

### Days out of role

Respondents with epilepsy reported a significantly higher mean number of days in the past 30 than other respondents when they were completely unable to conduct their daily activities because of their health (2.0 vs. 0.6,  $p = .001$ ) as well as significantly higher mean days of reduced work quality (4.0 vs. 1.9,  $p = .003$ ) and quantity (3.4 vs. 1.3,  $p = .003$ ). Controlling for socio-demographics, these differences are equivalent to unstandardized linear regression coefficients of 1.2–1.8 ( $p = .005-.010$ ). (Table 5) When we add controls for comorbid disorders, the coefficients remain statistically significant for days out of role (0.8,  $p = .045$ ) and total days of role impairment (1.8,  $p = .022$ ), but not days of reduced quality or quantity ( $p = .07-.17$ ). Based on the US Census population estimate of 232 million adults aged 18+ during the time of NCS-R data collection ([www.census.gov/popest/national](http://www.census.gov/popest/national)), the annualized population projection from the final adjusted model is 89.4 million total days of role impairment associated with epilepsy controlling for comorbid disorders. Interactions of epilepsy with number of comorbid physical and mental disorders in predicting days out of role measures are consistently insignificant ( $p = .46-.78$ ).

## DISCUSSION

The 1.8% lifetime prevalence estimate of self-reported medically recognized epilepsy in the NCS-R is within the 1.2–2.0% range found in previous US general population surveys using similar case definitions.<sup>8, 17, 30–33</sup> Given the complexities of epilepsy diagnosis, such self-reports are likely to be over-inclusive, capturing people with other paroxysmal or neurological conditions in addition to epilepsy. Based on the positive predictive values of 69–81.5% in previous validation studies,<sup>19, 20</sup> 20–30% of NCS-R respondents classified with epilepsy are likely to be false positives.

Our failure to detect significant associations of epilepsy with sex or race-ethnicity is consistent with previous studies.<sup>8, 17, 33, 34</sup> Although age-specific elevations have previously been observed among children and the elderly, we did not expect them in the NCS-R owing to the absence of children and the relatively small sub-sample of elderly in the sample. Although we failed to confirm prior associations of epilepsy with low education,<sup>17, 35</sup> a non-



significant trend was found. The findings that NCS-R respondents with epilepsy were much more likely than others to remain unmarried and, if ever married, to divorce are also consistent with previous surveys.<sup>33, 36, 37</sup>

Our finding of significant comorbidity between epilepsy and many other chronic physical disorders is broadly consistent with other surveys in the US,<sup>7, 15, 33</sup> Canada,<sup>9</sup> and Europe.<sup>38, 39</sup> Specific patterns of comorbidity are also consistent with earlier studies, confirming especially high comorbidities with neurological<sup>10, 38</sup> (stroke, multiple sensory impairments, headache) and functional or rheumatologic (asthma, digestive disorders, and arthritis) disorders.<sup>31</sup> Although causal pathways in these comorbidities are not fully understood, chronic antiepileptic drug use has been implicated in comorbidity between epilepsy and digestive disorders,<sup>18</sup> while increased nicotine use has been implicated in comorbidity between epilepsy and respiratory disorders.<sup>17, 31, 32, 38</sup> Although it is not clear why we found that comorbidity of epilepsy with physical disorders is largely due to *high* comorbidity, this is a striking result that warrants further investigation.

The generally positive pattern of comorbidity between epilepsy and mental disorders in the NCS-R is broadly consistent with previous epidemiological<sup>7, 8, 16–18</sup> and clinical<sup>40–42</sup> studies, as is the finding that comorbidity is stronger with physical than mental disorders.<sup>38, 43</sup> It is unclear, though, why significant associations of epilepsy with mental disorders are limited to panic disorder, PTSD, and conduct disorder, as one would normally expect associations with disorders to generalize to other strongly related disorders (i.e., phobias with panic disorder, major depression and generalized anxiety disorder with PTSD, and all other behavior disorders with conduct disorder). This idiosyncratic NCS-R profile raises the possibility that the significant ORs of epilepsy with panic disorder, PTSD, and conduct disorder might reflect diagnostic confusions of a sort that has been documented in clinical studies.<sup>44–46</sup> The uniformly elevated associations of epilepsy with substance use disorders, in comparison, are consistent with previous findings of decreased seizure threshold related to alcohol<sup>47</sup> and recreational drug<sup>10</sup> use/withdrawal.

Our finding of a very strong unadjusted OR between epilepsy and disability (6.6) is broadly consistent with previous studies.<sup>33, 48, 49</sup> Even though this OR decreased substantially when we controlled for comorbidity, the net OR of 3.8 remains very substantial, suggesting indirectly that epilepsy has important adverse effects on employment independent of comorbid disorders. The finding that epilepsy is positively associated with impairments in all WHO-DAS domains is broadly consistent with previous findings of substantial functional impairment in epilepsy.<sup>4, 6, 7</sup> However, the finding that all but one of these significant associations are explained by controls for comorbid disorders was unexpected, especially in light of the subsequent finding of significant net associations of epilepsy with days of role impairment. The finding of a significant net association of epilepsy impairment in cognition is consistent with experimental and clinical evidence of deficits among epileptics across multiple cognitive domains that have broad implications for psychological adjustment and daily life.<sup>50</sup>

We are aware of no previous research that examined associations of epilepsy with days of role impairment. The excess days out of role and of reduced work quantity and quality in the gross analyses are substantial in comparison to estimates obtained in previous studies of other chronic conditions.<sup>21</sup> Although these gross associations are reduced substantially by controls for comorbid disorders, the net association with overall days of role impairment remains both statistically and substantively significant, with an annualized equivalent of 89.4 million days of role impairment associated with epilepsy in the US adult population.

The discrepancy between the generally insignificant net associations of epilepsy with WHO-DAS scores and the significant net associations of epilepsy with disability and days of role impairment is striking. This discrepancy might be related to the documented incongruence between epilepsy patients' objective recognition of the implications of their symptoms (which would presumably be reflected in their reports of days of role impairment) and their dampened subjective evaluation of these implications.<sup>51, 52</sup> It is important to recognize in this regard that the WHO-DAS scores are subjective ratings of severity of impairment. Another indication that epilepsy is associated with a marked disjunctions between subjective evaluation and objective personal circumstances is that while respondents with epilepsy reported only modest decrements in social role functioning that were entirely explained by comorbid conditions, these same respondents were objectively and significantly less likely than others to have ever married and, if ever married, nearly twice as likely as others to be divorced at the time of interview.

The fact that the net associations of epilepsy with the various outcomes considered here all became smaller, and in the case of the WHO-DAS outcomes largely insignificant, when comorbid disorders were controlled raises the possibility that causal effects of epilepsy on these outcomes are *mediated* by comorbid disorders. However, there are two other plausible scenarios that could account for the observed associations: that comorbid disorders cause both epilepsy and impairments; and that unmeasured common causes led both to epilepsy and comorbid disorders as well as to impairments. We have no way to adjudicate among these different possibilities with the non-experimental cross-sectional NCS-R data. To the extent that mediation is at work, though, interventions aimed at reducing the onset and severity of secondary comorbid disorders might help reduce the impairments associated with epilepsy even though substantial impairments associated with work disability and days out of role remain even after controlling all comorbid disorders.

These conclusions should be interpreted in light of several limitations. The most obvious of these is that epilepsy was assessed with self report. It is reassuring in this regard that recent clinical reappraisal studies in community samples demonstrated good sensitivity and positive predictive value of epilepsy self reports when compared to consensus medical diagnoses.<sup>19, 20</sup> Nonetheless, caution is needed in interpreting our results due to the likelihood of misclassification of some cases. We also lacked data on specific seizure parameters, although empirical support for associations between highly textured seizure variables such as localization and lateralization and comorbidities remains equivocal.<sup>42, 53</sup> Another limitation is that while the CIDI provides validated data on DSM-IV disorders overall, it may overestimate comorbidity of mental disorders among people with epilepsy due to the coarseness with which organic exclusions are assessed. The cross-sectional design of the NCS-R and absence of data on age of onset are additional design limitations that precluded the direct confirmation of temporal associations between epilepsy and comorbid disorders. The small number of NCS-R respondents classified as having epilepsy ( $n = 135$ ) is another limitation, as it made it impossible to carry out sub-group analyses with adequate statistical power. The large number of tests, finally, raises concerns about the possibility that some of the significant net associations could be false positive findings. This might explain the one significant interaction out of 16 between epilepsy and number of comorbid disorders in predicting WHO-DAS scores.

Despite these limitations, the data reported here demonstrate clearly that epilepsy is associated with numerous role impairments and that impairments associated with work disability and days out of role remain significant in both statistical and substantive terms even after adjusting statistically for a wide range of physical and mental comorbidities. To the extent that epilepsy causes any of the comorbid disorders considered here and to the extent that comorbid mental disorders are actually seizure epiphenomena, the true effects of



epilepsy on these role impairments are likely to be even greater larger than the net associations documented here. Based on these results, it seems safe to conclude that role impairments are major components of the societal costs of epilepsy rather than due entirely to comorbid disorders.

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**Table 1**

Comorbidity of epilepsy with lifetime physical disorders among Part II NCS-R respondents (n = 5,692)

	<u>Prevalence of physical disorder<sup>1</sup></u>				<u>Odds-Ratios<sup>2</sup></u>	
	<u>With Epilepsy</u>		<u>Without Epilepsy</u>		<u>OR</u>	<u>(95% CI)</u>
	<u>%</u>	<u>(se)</u>	<u>%</u>	<u>(se)</u>		
I. Cardiovascular						
Heart attack	5.4	(2.2)	3.6	(0.4)	1.5	(0.6–3.8)
Heart disease	6.7	(2.4)	5.0	(0.4)	1.5	(0.6–3.5)
High blood pressure	30.4	(5.9)	23.9	(0.6)	1.5	(0.8–2.8)
Stroke	8.0	(2.5)	2.6	(0.3)	3.0*	(1.4–6.5)
Any cardiovascular	34.6	(5.7)	27.9	(0.6)	1.5	(0.8–2.8)
II. Digestive						
Irritable bowel	7.9	(4.6)	3.1	(0.3)	2.1	(0.7–6.0)
Ulcer	14.2	(2.8)	9.3	(0.5)	1.4	(0.9–2.4)
Any digestive	22.2	(5.4)	11.8	(0.5)	1.9*	(1.0–3.3)
III. Musculoskeletal						
Arthritis	35.8	(5.0)	27.1	(0.9)	1.6*	(1.0–2.4)
Back or neck	39.3	(5.2)	29.1	(0.9)	1.5	(0.9–2.2)
Any musculoskeletal	53.6	(6.4)	42.2	(0.9)	1.6	(1.0–2.7)
IV. Pain disorders						
Migraines	7.6	(2.0)	5.6	(0.4)	1.2	(0.7–2.1)
Other headaches	29.6	(4.0)	16.9	(0.6)	1.8*	(1.2–2.7)
Other pain	18.2	(5.9)	9.4	(0.4)	1.8	(0.8–4.0)
Any pain disorder	69.9	(6.8)	53.2	(1.0)	2.0*	(1.1–3.8)
V. Respiratory						
Asthma	25.7	(6.2)	11.4	(0.6)	2.2*	(1.2–4.3)
Seasonal allergies	45.0	(6.2)	37.5	(1.2)	1.3	(0.8–2.2)
Other lung disorders (e.g., COPD, TB)	5.7	(2.2)	2.1	(0.3)	2.0	(0.8–5.1)
Any respiratory disorder	58.9	(4.8)	42.5	(1.2)	1.8*	(1.2–2.7)
VI. Sensory						

	Prevalence of physical disorder <sup>1</sup>				Odds-Ratios <sup>2</sup>	
	With Epilepsy		Without Epilepsy		OR	(95% CI)
	%	(se)	%	(se)		
Blind or vision impairment	9.0	(2.8)	3.1	(0.3)	2.2 *	(1.2–4.2)
Deaf or hearing impairment	9.4	(2.9)	3.7	(0.3)	2.8 *	(1.3–6.2)
Any sensory disorder	15.9	(3.5)	6.1	(0.3)	2.7 *	(1.5–4.9)
VII. Other disorders						
Cancer	6.6	(2.6)	6.6	(0.5)	1.2	(0.4–3.4)
Diabetes	11.8	(5.2)	7.1	(0.4)	1.4	(0.5–3.9)
VIII. Total						
Any of the above disorders	93.6	(1.7)	77.8	(1.0)	4.2	(2.2–7.9)
Exactly one	18.7	(5.0)	23.6	(0.9)	2.4	(1.0–5.8)
Exactly two	22.7	(4.4)	19.7	(0.8)	4.4	(2.0–9.3)
Exactly three	11.0	(2.5)	14.3	(0.6)	3.1	(1.2–7.8)
Four or more	41.2	(5.9)	20.2	(0.7)	6.2	(2.5–15.0)

\* Significant at the .05 level, two-sided test

<sup>1</sup> Prevalence of the physical disorder separately among respondents with and without epilepsy

<sup>2</sup> Based on a series of multivariate logistic regression models in which epilepsy predicted each physical disorder with controls for age, age-squared, sex, and race-ethnicity



**Table 2**

Comorbidity of epilepsy with lifetime DSM-IV/CIDI mental disorders among Part II NCS-R respondents (n = 5,692)

	Prevalence of mental disorder <sup>1</sup>				Odds-Ratios <sup>2</sup>	
	With Epilepsy		Without Epilepsy		OR	(95% CI)
	%	(se)	%	(se)		
I. Anxiety disorders						
Generalized Anxiety Disorder	8.4	(2.4)	5.7	(0.3)	1.3	(0.7–2.6)
Specific phobia	19.3	(4.2)	12.5	(0.5)	1.4	(0.8–2.6)
Social phobia	15.7	(3.2)	12.1	(0.4)	1.1	(0.7–1.9)
Panic disorder	10.3	(2.5)	4.6	(0.3)	1.9*	(1.0–3.6)
Agoraphobia	1.0	(0.7)	1.4	(0.1)	0.5	(0.1–2.1)
Adult separation anxiety disorder	6.7	(1.8)	6.6	(0.3)	0.7	(0.4–1.4)
Child separation anxiety disorder	6.0	(2.0)	4.1	(0.3)	1.1	(0.5–2.5)
Posttraumatic stress disorder	16.0	(3.0)	6.7	(0.4)	2.0*	(1.2–3.3)
Any anxiety disorder	40.7	(4.9)	30.8	(1.0)	1.3	(0.8–2.1)
II. Mood disorders						
Major depressive disorder	20.6	(3.8)	16.8	(0.6)	1.1	(0.7–1.7)
Dysthymic disorder	5.8	(1.7)	2.4	(0.2)	1.8	(0.9–3.7)
Bipolar disorder <sup>3</sup>	4.9	(1.6)	4.4	(0.3)	0.9	(0.4–1.8)
Any mood disorder	25.9	(3.9)	21.3	(0.7)	1.0	(0.7–1.6)
III. Disruptive behavior disorders						
Intermittent explosive disorder	9.8	(2.9)	7.3	(0.4)	1.4	(0.7–2.6)
Attention deficit-hyperactivity disorder	4.9	(1.7)	4.2	(0.3)	1.0	(0.5–2.1)
Oppositional-defiant disorder	3.7	(1.7)	4.5	(0.4)	0.7	(0.2–2.2)
Conduct disorder	13.8	(5.0)	4.8	(0.4)	3.3*	(1.5–7.3)
Any disruptive behavior disorder	24.6	(4.9)	14.8	(0.7)	1.9*	(1.1–3.2)
IV. Substance disorders <sup>4</sup>						
Alcohol abuse	20.6	(4.5)	13.1	(0.6)	1.6	(0.9–2.8)
Alcohol dependence with abuse	9.5	(3.1)	5.3	(0.3)	1.7	(0.8–3.5)
Drug abuse	14.9	(3.9)	7.8	(0.4)	1.8*	(1.0–3.4)

	Prevalence of mental disorder <sup>1</sup>				Odds-Ratios <sup>2</sup>	
	With Epilepsy		Without Epilepsy		OR	(95% CI)
	%	(se)	%	(se)		
Drug dependence with abuse	5.0	(1.6)	3.0	(0.2)	1.4	(0.7–2.8)
Any substance disorder	23.8	(5.0)	14.5	(0.6)	1.7	(0.9–3.0)
V. Total						
Any of the above disorders	67.9	(6.1)	47.0	(1.1)	2.1*	(1.2–3.7)
Exactly one	18.6	(4.8)	18.1	(0.6)	1.6	(0.7–3.7)
Exactly two	17.4	(3.1)	10.1	(0.5)	2.5*	(1.3–4.9)
Three or more disorders	31.9	(4.8)	18.7	(0.7)	2.5*	(1.3–4.7)

\* Significant at the .05 level, two-sided test

<sup>1</sup> Prevalence of the mental disorder separately among respondents with and without epilepsy

<sup>2</sup> Based on a series of multivariate logistic regression models in which epilepsy predicted each physical disorder with controls for age, age-squared, sex, and race-ethnicity

<sup>3</sup> Bipolar I or bipolar II or sub-threshold Bipolar disorder

<sup>4</sup> Abuse is defined with or without dependence

**Table 3**

The association (odds-ratio) between epilepsy and work disability among Part II NCS-R respondents in the labor force (n = 4,332)<sup>1</sup>

Controls	Odds-Ratios <sup>2</sup>	
	OR	(95% CI)
None	6.6 *	(3.6–11.8)
Socio-demographics <sup>3</sup>	5.7 *	(3.4–9.5)
Socio-demographics <sup>3</sup> , physical disorders	4.1 *	(2.2–7.5)
Socio-demographics <sup>3</sup> , mental disorders	5.0 *	(3.0–8.3)
Socio-demographics <sup>3</sup> , physical and mental disorders	3.8 *	(2.2–6.7)

\* Significant at the .05 level, two-sided test

<sup>1</sup> The prevalence (standard error) of disability is 33.1% (7.2) among respondents in the labor force with epilepsy and 7.0% (0.6) among other respondents (t = 3.6, p < .01).

<sup>2</sup> Based on a series of multivariate logistic regression models that predicted disability from epilepsy with controls for age, age squared, sex, and race-ethnicity and subsequently controls either for physical disorders (a separate dummy variable for each disorder reported plus a linear term for number of such disorders and a quadratic term for the square of the number of disorders), mental disorders (coded in the same way as for physical disorders), or both physical and mental disorders. An additional model was estimated that added interactions of epilepsy with number of physical and number of mental disorders, but these interactions were not statistically significant ( $\chi^2_2 = 3.2$ , p = .20).

<sup>3</sup> Age, age squared, sex, and race-ethnicity.

Table 4

The associations (unstandardized linear regression coefficient) between epilepsy and summary WHO-DAS scores in the 30 days before interview among Part II NCS-R respondents (n = 5,692)<sup>1</sup>

Controls	Basic Activities of Daily Living			Outcomes <sup>2</sup> Instrumental Activities of Daily Living			Societal Response		
	Self care	Cognition	Mobility	Productive role functioning	Social role functioning	Discrimination	Family burden	Stigma	
	b (se)	b (se)	b (se)	b (se)	b (se)	b (se)	b (se)	b (se)	
None	1.8 (1.1)	3.6* (1.0)	7.9 (3.7)	15.8* (4.9)	1.4 (0.6)	2.5* (1.2)	5.1* (1.5)	6.8* (2.6)	
Socio-demographics <sup>3</sup>	0.8 (1.1)	3.1* (1.0)	5.1 (3.1)	10.6* (3.8)	1.0 (0.6)	1.8 (1.2)	3.5* (1.6)	5.6* (2.4)	
Socio-demographics, <sup>3</sup> physical disorders	0.2 (1.0)	2.5* (1.1)	2.8 (2.9)	6.6 (3.6)	0.6 (0.6)	1.2 (1.3)	2.1 (1.8)	4.2 (2.3)	
Socio-demographics, <sup>3</sup> mental disorders	0.8 (1.0)	2.8* (1.0)	4.5 (3.1)	9.0* (4.0)	0.7 (0.5)	1.4 (1.2)	2.7 (1.6)	4.9* (2.4)	
Socio-demographics, <sup>3</sup> physical and mental disorders	0.2 (1.0)	2.4 (1.0)	2.6 (2.9)	5.8 (3.7)	0.4 (0.5)	1.0 (1.2)	1.8 (1.7)	3.9 (2.3)	

\* Significant at the .05 level, two-sided test

<sup>1</sup> Based on a series of multivariate linear regression models that predicted the outcomes from epilepsy with controls for age, age squared, sex, and race-ethnicity and subsequently controls either for physical disorders (a separate dummy variable for each disorder reported plus a linear term for number of such disorders and a quadratic term for the square of the number of disorders), mental disorders (coded in the same way as for physical disorders), or both physical and mental disorders. An additional model was estimated that added interactions of epilepsy with number of physical and number of mental disorders. The pair of interactions was significant as a set in predicting self-care ( $F_{2,5645} = 3.3, p = .047$ ) due to a significant negative interaction between epilepsy and number of mental disorders ( $F_{1,5645} = 6.0, p = .018$ ). The interaction between epilepsy and number of physical disorders, in comparison, was not significant ( $F_{1,5645} = 0.6, p = .44$ ) in predicting self-care. None of the other 14 interactions predicting the other 7 WHO-DAS outcomes was individually significant ( $F_{1,5645} = 0.1-2.1, p = .15-.94$ ). Nor was any of the other 7 two degree of freedom tests significant ( $F_{2,5645} = 0.1-1.9, p = .16-.90$ ).

<sup>2</sup> The prevalence estimate (standard error) of each outcome among respondents with and without epilepsy is as follows: Days out of role 2.0 (0.4) vs. 0.6 (0.0) ( $t = 2.2, p = .022$ ); Days with reduced work quality 4.0 (0.6) vs. 1.9 (0.1) ( $t = 5.7, p < .001$ ); Days with reduced work quantity 3.4 (0.6) vs. 1.3 (0.1) ( $t = 5.7, p < .001$ ); total days of role impairment 5.4 (0.7) vs. 2.2 (0.1) ( $t = 6.4, p < .001$ ).

<sup>3</sup> Age, age squared, sex, and race-ethnicity.

The associations (unstandardized linear regression coefficient) between epilepsy and WHO-DAS measures of days of impaired role functioning in the 30 days before interview among Part II NCS-R respondents (n = 5,692)<sup>1</sup>

Table 5

	Outcomes <sup>2</sup>					
	Days out of role		Reduced quality		Reduced quantity	
	b	(se)	b	(se)	b	(se)
<b>Controls</b>						
None	1.4*	(0.4)	2.1*	(0.6)	2.1*	(0.6)
Socio-demographics <sup>3</sup>	1.2*	(0.4)	1.7*	(0.6)	1.8*	(0.6)
Socio-demographics, <sup>3</sup> physical disorders	1.0*	(0.4)	1.4*	(0.6)	1.5*	(0.6)
Socio-demographics, <sup>3</sup> mental disorders	0.9*	(0.4)	1.1	(0.6)	1.3*	(0.6)
Socio-demographics, <sup>3</sup> physical and mental disorders	0.8*	(0.4)	0.8	(0.6)	1.2	(0.6)

\* Significant at the .05 level, two-sided test

<sup>1</sup>Based on a series of multivariate linear regression models that predicted the outcomes from epilepsy with controls for age, age squared, sex, and race-ethnicity and subsequently controls either for physical disorders (a separate dummy variable for each disorder reported plus a linear term for number of such disorders and a quadratic term for the square of the number of disorders), mental disorders (coded in the same way as for physical disorders), or both physical and mental disorders. An additional model was estimated that added interactions of epilepsy with number of physical and number of mental disorders. These interactions were not statistically significant ( $F_{2,5645} = 0.2-0.8, p = .46-.78$ ).

<sup>2</sup>The prevalence estimate (standard error) of each outcome among respondents with and without epilepsy is as follows: Days out of role 2.0 (0.4) vs. 0.6 (0.0) ( $t = 2.2, p = .022$ ); Days with reduced work quality 4.0 (0.6) vs. 1.9 (0.1) ( $t = 5.7, p < .001$ ); Days with reduced work quantity 3.4 (0.6) vs. 1.3 (0.1) ( $t = 5.7, p < .001$ ); total days of role impairment 5.4 (0.7) vs. 2.2 (0.1) ( $t = 6.4, p < .001$ ).

<sup>3</sup>Age, age squared, sex, and race-ethnicity.